Critical Regulatory Controls within Pharmaceutical Corporation

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***Abstract*— Access to healthcare is a fundamental human right. It is the government's responsibility to provide authentic medicines and a robust healthcare system as an integral aspect of human life. Currently, many governments worldwide are implementing various welfare schemes to ensure quality healthcare services as a fundamental right. The pharmaceutical industry is also recognized as a vital component of healthcare services, continually innovating to enhance people's well-being.**

New research and its potential outcomes are instilling new hope for curing critical and rare diseases. The pharmaceutical industry must embrace innovative technologies within its enterprise systems to manage the entire drug development process, from research through final approval. Enterprise systems safeguard research data and patient confidentiality, uphold Good Manufacturing Practice (GMP) standards during production, enabling the creation of groundbreaking medicines that improve human life expectancy and overall quality of life. These systems also provide accurate information for both internal and external audits.

In the pharmaceutical business process, enterprise systems effectively reduce defects and facilitate Corrective and Preventive Actions (CAPA). The development of new drugs and alternatives to expensive medications is offering cost-effective and accessible treatment options for underserved populations. However, the adoption of new technologies in enterprise systems and the improvement of existing infrastructure present significant challenges, particularly in economically disadvantaged and developing countries.

The intricate and protracted process of drug development, coupled with substantial research and development investments, becomes more precarious when results fail to yield substantial health improvements. Newly launched drugs often prove to be prohibitively expensive for patients in need, exerting immense pressure on healthcare budgets. These trends raise pertinent questions about the incentives within the pharmaceutical sector and the sustainability of current pricing models."

The integration of novel technologies and the presentation of precise clinical trial findings are enhancing the efficiency of the drug development process, concurrently elevating the likelihood of obtaining approval. The stages of product development encompass numerous IT applications, each endowed with distinct functionalities. These systems necessitate interconnectivity to enable seamless data processing, validations, and result analysis. Some systems operate at the site level, handling data recording and activities, while others operate at a corporate level, catering to drug reports and analytical requirements.

Objective: This study intends to empirically describe the process of pharmaceutical drug launch and its readiness in enterprise systems.

Keywords— Essential controls of Pharmaceuticals; Corporation; Regulatory compliance; Pharmaceutical Barcode;

Serialization; Drug price controls; Master Data Governance

Introduction

- Pharmaceutical processes are subject to stringent regulations, requiring strict compliance throughout. The drug development life cycle undergoes rigorous scrutiny and mandated reporting at every stage of pharmaceutical operations, encompassing research and development (R&D), sales and marketing, fair pricing policies, patient health information confidentiality and security. This includes the reporting of adverse events during clinical trials, adherence to Good Manufacturing Practices (GMP), and the establishment of Standard Operating Procedures (SOP) for the incorporation of new business processes.

- The implementation of these highly regulated policies and rigorous audits ensures the delivery of high-quality healthcare services and pharmaceuticals to patients. Given the inherent risks of non-compliance and other threats to the pharmaceutical industry, drug developers must possess a comprehensive understanding of the regulatory bodies overseeing them. They need to stay informed about new regulatory guidelines and how these guidelines apply to their operations, while also prioritizing regulatory compliance at the enterprise system level.

Historical adverse events have prompted governments to focus urgently on medical affairs, resulting in policy changes aimed at providing more affordable healthcare services and drugs. Another contributing factor is the rapid globalization of the healthcare industry, coupled with increased drug accessibility due to advancements in digital supply chain management. Some organizations are enhancing their medical affairs services through process optimization. They are expanding training initiatives, adopting technologies and equipment to improve quality, and minimizing adverse events by incorporating enterprise systems capable of automating processes where necessary, reducing the need for manual intervention."

Pharm Regulatory Conformity and Compliance

- As per the FDA, the pharmaceutical quality control laboratory serves a pivotal role in pharmaceutical production and control. A substantial portion of the Current Good Manufacturing Practice (CGMP) regulations (21 CFR 211) pertains to the quality control laboratory and product testing. Thus, the quality control (QC) laboratory plays a central role in pharmaceutical manufacturing. Its testing procedures verify product quality, and the resulting reports serve as documentary evidence. Extensive volumes of data are generated during testing at various manufacturing stages, and this data should reveal whether quality has been consistently maintained throughout the process. Understandably, QC laboratory data undergoes rigorous regulatory scrutiny, as any inaccuracies could lead to the production of ineffective products or pose risks to patient safety. Additionally, such data can reflect the transparency of a company's systems.

- The integrity of QC data, including its completeness, consistency, and accuracy, is of paramount importance. It should be traceable, legible, contemporaneously recorded, either original or a true copy, and precise. Furthermore, it should be comprehensive, consistent, durable, and readily accessible. Many laboratory operations are managed using various business enterprise system tools, including Lab Execution Systems (LES) for guiding laboratory procedures and Scientific Data Management Systems (SDMS) for integrating instruments throughout the facility and centralizing data collection. Often, Laboratory Information Management Systems (LIMS) operate alongside these systems to provide insights into laboratory operations and identify any data trends that may indicate warnings or failures.

- However, there is a growing demand for a more unified approach to laboratory and data management. To meet current requirements, business enterprise systems offer a comprehensive solution with a complete informatics infrastructure that combines LIMS, SDMS, and LES. Consolidating all these capabilities within a single business enterprise system simplifies training and administration, streamlines compliance efforts, enhances overall quality control, and can be implemented across different geographic locations and partnerships for more comprehensive management.

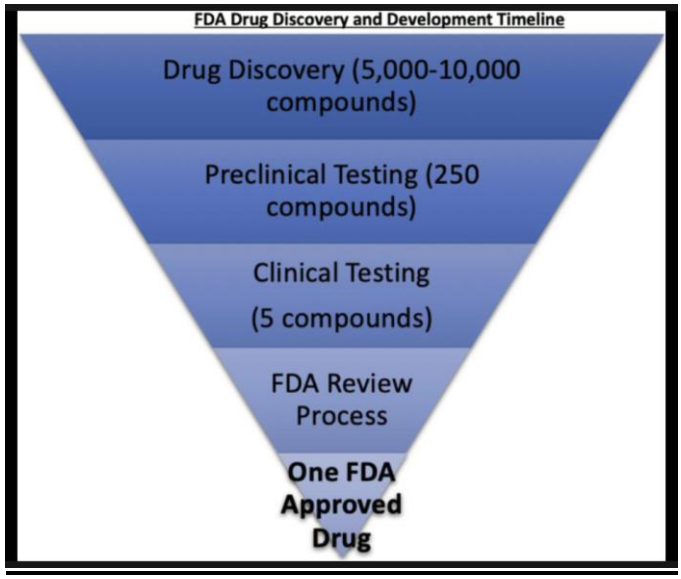
Pharmaceuticals - Noncompliance

- Noncompliance in the pharmaceutical industry is a critical issue that can have devastating effects on manufacturing and other business processes. Pharmaceutical manufacturing processes and supply chains are highly intricate. Companies, whether large or small, often rely partly or entirely on their contracted manufacturing partners. These interdependencies mean that any suspension of manufacturing at a contract manufacturing

site or supplier can impact their production and result in significant financial losses due to business interruptions. In the past, physical damage was considered the primary risk for business interruptions, but regulatory-based risks have gained prominence. Achieving growth and resilience by implementing business enterprise systems is a pivotal aspect of the strategic model in the pharmaceutical industry.

Any major manufacturing irregularity in compliance with Good Manufacturing Practices (GMP) is likely to trigger regulatory actions such as a Form 483, Warning Letter, or consent decree in the United States; withdrawal of manufacturing authorization in Europe; or an import ban. All of these actions result in major production interruptions while remediation efforts are undertaken to restore compliance. The loss of manufacturing capacity due to regulatory non-compliance can have a severe impact on biopharmaceutical or medical device manufacturers and can occur at any point along a company's supply chain. Implementing business enterprise systems in GMP areas, such as the production floor and quality assurance/quality control (QA/QC) areas, ensures a defect-free environment.

Pharmaceutical Approval Procedure



- In the United States, the Food and Drug Administration (FDA) issued a Compliance Policy Guide (CPG) titled "Marketed Unapproved Drugs" on September 19, 2011. This CPG represents a revision of the FDA's 2006 CPG addressing the same subject matter. Notably, this CPG not only outlines the FDA's current stance on enforcement actions related to these drugs but also elucidates the process by which manufacturers can voluntarily submit a New Drug Application (NDA).

- The CPG introduces several categories of marketed unapproved drugs that the FDA considers enforcement priorities. Aligned with the FDA's overarching objective of ensuring that all products adhere to the approval requirements stipulated in the Federal Food, Drug, and Cosmetic Act (FDCA)—specifically, that all drug products demonstrate both safety and effectiveness—the FDA has identified the following as priority products:

- Drugs associated with potential safety risks.
- Drugs lacking evidence of effectiveness.
- "Health Fraud Drugs," signifying drugs that have not been substantiated as safe and effective for their claimed benefits.
- Drugs presenting challenges to the NDA or over-the-counter (OTC) review systems.
- Drugs contravening the FDCA in various ways.
- Drugs that have been reformulated to evade FDA action but remain noncompliant.

- Within this context, the FDA has indicated its intention to assess products on a case-by-case basis to determine whether a period of continued marketing is justified. Consequently, the existence of a "grace period" is contingent upon factors such as its impact on the public, the feasibility of conducting requisite scientific studies, the burden on affected parties, the FDA's resource constraints, and other exceptional circumstances. Moreover, the CPG outlines a unique circumstance where the variable grace period described above may inadvertently result in a de facto exclusivity period for the first manufacturer to comply with the FDCA.

- The FDA acknowledges that a company may file an NDA for a product that other companies are marketing without approval. In such cases, the FDA typically intends to allow a one-year grace period before initiating any enforcement actions against unapproved drugs that remain available in the market. Nevertheless, it is important to note that this one-year period is not fixed and will be determined on a case-by-case basis. As specified in the CPG, "the shorter the grace period, the more likely it is that the first company to obtain approval will have a period of de facto market exclusivity before other products gain approval."

- Pharmaceutical companies have the opportunity to optimize their operations by investing in enterprise systems, enabling them to identify and divest non-strategic assets to interested buyers who can then continue supplying finished products to the seller. This approach can assist smaller manufacturers in addressing budgetary constraints and raising funds for the implementation of enterprise systems to mitigate the risk of defects.

To minimize potential risks, the seller has requested that the buyer furnish evidence demonstrating their capability to financially manage potential losses and replacements for supplied products in the event of manufacturing errors. Such errors could lead to product wastage and shortages, underscoring the need for financial safeguards.

Quality Audit

- A pharmaceutical quality audit represents a vital and mandatory systematic and independent analysis of data and tasks to ascertain compliance with established regulations. It serves the dual purpose of determining whether these activities are not only compliant but also effectively implemented to achieve the specified objectives. Quality audits, whether conducted internally or externally, are integral components of a robust pharmaceutical quality management system. Through quality audits, pharmaceutical companies can thoroughly assess their compliance with regulatory requirements and gain invaluable feedback for continuous improvement.

Internal Auditing

- Internal auditing is an independent and objective assurance and consulting activity meticulously designed to enhance organizational operations. In the context of EU member states, it is often referred to as "self-inspection," while ISO 9000:2000 defines it as "measurement, analysis, and improvement." The internal audit process is conducted by an entity on its own systems, procedures, and facilities, with internal auditors employed by the distributor. In the United States, compliance with the Sarbanes-Oxley Act (SOX), a significant federal law, is of critical importance. SOX enhances transparency in financial reporting and formalizes enterprise systems for internal controls. Pharmaceutical companies utilize SOX controls through their enterprise systems to safeguard against financial data breaches and revenue losses. Another vital regulatory compliance is found in 21 CFR Part 11, which governs the United States Food and Drug Administration's regulations concerning electronic records and electronic signatures. Business enterprise systems are proficient in storing all audit logs and authenticating transactions via electronic signatures.

- As a pharmaceutical company, you must conduct audits of your facilities, systems, and Standard Operating Procedures (SOPs) through the process of internal auditing. These audits are conducted at regular intervals, and comprehensive procedures and programs must be in place for their execution.

- The complexity of internal auditing processes can be categorized into multiple tiers:

- Tier 1: These audits are the least complex and are typically conducted by personnel from the relevant department or section. They are of relatively short duration, conducted frequently, and focus on issues such as the assessment of housekeeping or documentation within a specific department or section.

- Tier 2: Tier 2 internal audits are more intricate compared to Tier 1 audits. They place greater emphasis on the entire system and occur less frequently. These audits are characterized by longer durations, and auditors are required to undergo rigorous training, with a specific focus on quality systems and techniques. Importantly, auditors in Tier 2 are independent of the department or section being audited.

- Tier 3: Tier 3 internal audits represent the most complex and least frequent category. They may be conducted to assess the pharmaceutical company's readiness for an impending regulatory audit or before initiating a critical activity. Auditors for Tier 3 internal audits must possess advanced training and comprehensive knowledge of all regulatory requirements within the pharmaceutical industry.

- External Auditing

- Pharmaceutical companies routinely engage in external audits to ensure that their operations align with established guidelines. These audits encompass various categories:

- Financial Audit: This review assesses the accuracy of the company's financial statements by evaluating fiscal solvency with respect to assets and liabilities.

- Compliance Audit: A compliance audit examines the degree of conformity with operating procedures as stipulated by contractual arrangements and government regulatory agencies. It includes an investigation into hard-copy prescriptions, computerized refill records, and invoice records.

- Operational Audit: Also known as a performance or management audit, it seeks to evaluate the overall efficiency of the company as a provider of prescription plans for various sponsors.

- The audit process commences with an opening meeting to introduce auditors to the company's management, explain the audit rationale, review scope and objectives, and agree on the agenda and timeline. Any confidentiality issues, such as safety protocols, photography, and sample collection, are clarified. Auditors observe, question, examine documentation and records, and address concerns to obtain evidence of compliance. In compliance audits, drugs produced by the company are tested to ensure they contain the required medication as mandated by law. Expenses, particularly research and development costs related to new drugs, are scrutinized. Additionally, the integrity and adequacy of internal controls that prevent inappropriate actions by company employees are evaluated. Observations are recorded, and concerns are discussed with the auditee.

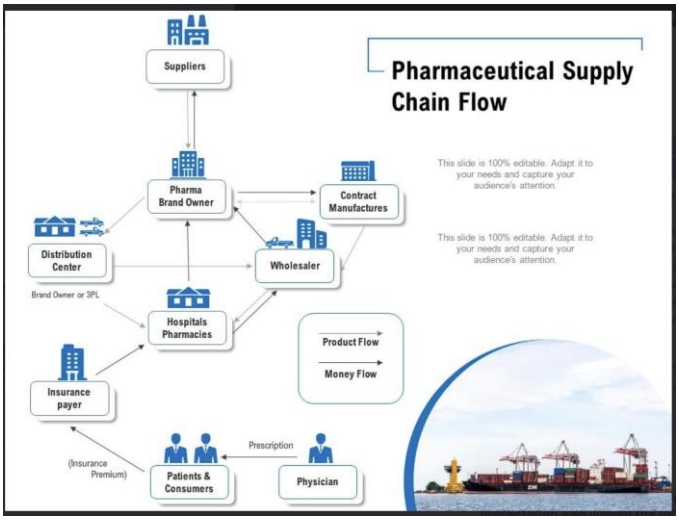
External audits also encompass monitoring sales data and controlling the distribution of medicine through legal supply chains. These measures serve to mitigate the risk of potential drug counterfeiting within illicit and black markets.

- The pharmaceutical supply chain plays a critical and integral role in the pharmaceutical business process. Any adverse event occurring within this supply chain not only affects the potency and shelf life of drugs due to delays but also poses a potential threat to patients' lives by impeding access to essential medications due to shortages [Reference 13]. The implementation of digital traceability for pharmaceutical drugs within the supply chain has proven to be a highly effective process for minimizing the risk associated with counterfeit and illicit drugs in the market [References 14, 15]. Additionally, the adoption of blockchain technology can be employed to establish a resilient end-to-end digital tracking system throughout the supply chain [Reference 16].

- Ensuring the accurate encoding of GS1 barcodes on pharmaceutical packages is essential for regulatory compliance, as mandated by the Healthcare Distribution Alliance (HDA). This compliance ensures the accuracy of information transmission across the supply chain [Reference 17]. Presently, the U.S. Food and Drug Administration (FDA) is conducting several pilot projects to assess the viability of blockchain technologies in completely mitigating the risks associated with counterfeit or illicit drugs within the supply chain [Reference 18]. Under these pilot projects, the Drug Supply Chain Security Act (DSCSA) is being evaluated to determine whether blockchain technology can be utilized for saleable return transactions within an interoperable network.

In the broader context, the pharmaceutical industry operates with disciplined and highly regulated business processes. The adoption of enterprise systems within the pharmaceutical industry is considered the most effective means of recognizing and tracking every individual raw material, from receipt through processing, packaging, and shipping to specific client locations. In the pharmaceutical industry, as well as the medical device and biotech sectors, product quality issues hold profound significance and can, quite literally, determine the difference between life and death. Organizations within this industry operate within one of the world's most rigorously regulated sectors, with regulations impacting various facets such as research and development, product development, traceability, quality management, and

reporting. To remain competitive and thrive within this demanding environment, pharmaceutical companies must conduct thorough assessments and develop a profound understanding of enterprise systems capable of monitoring production, procurement, documentation, and traceability—all while effectively managing compliance requirements.



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